## REMARKS

Initially, we note that previously presented claims 14 and 15 have not been rejected on any grounds and are, therefore, assumed to be allowed. If the Applicants' assumption is wrong, the Examiner is requested to reissue the Office Action and to formally identify the reasons for rejection on the record.

Claim 1 has been amended to recite "[a] vector or plasmid comprising an isolated DNA encoding vitamin $B_6$ phosphate phosphatase selected from the group consisting of:

(a) a DNA sequence of SEQ ID NO:9;

(b) a DNA sequence encoding a polypeptide having vitamin $B_6$ phosphate phosphatase activity, which hybridizes under stringent hybridization and stringent washing conditions to the DNA sequence defined in (a) or a fragment thereof, wherein the stringent hybridization and stringent washing conditions comprise hybridizing in 5xSSC, 0.3% SDS, 2% blocking reagent, 0.1% N-lauroylsarcosine, 50% formamide overnight at 42° C and washing twice in 2xSSC, 0.1% SDS at room temperature for 5 minutes and then washing twice in 0.1xSSC, 0.1% SDS at 50° C to 68° C for 15 minutes;

(c) a DNA sequence encoding a polypeptide having vitamin $B_6$ phosphate phosphatase activity, wherein said polypeptide is at least 95% identical to the amino acid sequence of SEQ ID NO:10;

(d) a DNA sequence encoding a polypeptide having vitamin $B_6$ phosphate phosphatase activity and is at least 95% identical to the DNA sequence of SEQ ID NO:9; and

(e) a degenerate DNA sequence of any one of (a) to (c)." Support for these amendments is found in the specification at, for example, page 3, lines 8-25; in Examples 1-2; and in original claim 1. *See In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01(o) and (I) (8th ed. Rev. 6, Sept. 2007, pp. 600-92 and 600-84).

Claim 4 has been amended to recite "[a] recombinant microorganism of the genus *Sinorhizobium* or *Escherichia*, capable of producing vitamin $B_6$ from vitamin $B_6$ phosphate, wherein said microorganism is transformed with a DNA encoding vitamin $B_6$ phosphate phosphatase selected from the group consisting of:

(a) a DNA sequence of SEQ ID NO:9;

(b) a DNA sequence encoding a polypeptide having vitamin $B_6$ phosphate phosphatase activity, which hybridizes under stringent hybridization and stringent washing conditions to the DNA sequence defined in (a) or a fragment thereof, wherein the stringent hybridization and stringent washing conditions comprise hybridizing in 5xSSC, 0.3% SDS, 2% blocking reagent, 0.1% N-lauroylsarcosine, 50% formamide overnight at 42° C and washing twice in 2xSSC, 0.1% SDS at room temperature for 5 minutes and then washing twice in 0.1xSSC, 0.1% SDS at 50° C to 68° C for 15 minutes;

(c) a DNA sequence encoding a polypeptide having vitamin $B_6$ phosphate phosphatase activity, wherein said polypeptide is at least 95% identical to the amino acid sequence of SEQ ID NO:10;

(d) a DNA sequence encoding a polypeptide having vitamin $B_6$ phosphate phosphatase activity and is at least 95% identical to the DNA sequence of SEQ ID NO:9; and

(e) a degenerate DNA sequence of any one of (a) to (c)." Support for these amendments is found in the specification at, for example, page 3, lines 8-25; in Examples 1-2; and in original claim 4. (*Id.*).

It is submitted that no new matter has been introduced by the foregoing amendments. Approval and entry of the amendments is respectfully solicited.

**Objections:**

The Examiner objected to claims 1 and 4, at part (b), line 2, because of the recitation "and hybridizes." (Paper No. 20070822 at 2). The Examiner suggested amending the phrase to recite "which hybridizes." (*Id.*).

As suggested by the Examiner, and with a view towards furthering prosecution, claims 1 and 4 have been amended to recite "which hybridizes" where appropriate. In view of these amendments, it is believed that the objection is rendered moot. Accordingly, withdrawal of the objection is respectfully requested.

**35 U.S.C. § 112, Second Paragraph, Rejection:**

Claims 1, 4-7, and 9-11 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. (*Id.*).

In making the rejection, the Examiner asserted that the phrase "stringent hybridization and stringent washing conditions" renders the claims indefinite. (*Id.*). The Examiner also asserted that "the specification does not define what conditions constitute 'stringent hybridization and stringent washing conditions.'" (*Id.*). The

Examiner further asserted that "[w]hile page 3 attempts to describe a stringent condition, the description is merely exemplary and not a clear definition. In the art the meaning of the term 'stringent' varies widely depending on the individual situation and the person making the determination. Therefore, it is not clear to the Examiner as to what hybridization and washing conditions are encompassed in the above phrase." (*Id.* at 3).

With a view towards furthering prosecution, claims 1 and 4 (from which claims 5-7 and 9-11, either directly or indirectly depend) have been amended to specifically recite "wherein the stringent hybridization and stringent washing conditions comprise hybridizing in 5xSSC, 0.3% SDS, 2% blocking reagent, 0.1% N-lauroylsarcosine, 50% formamide overnight at 42° C and washing twice in 2xSSC, 0.1% SDS at room temperature for 5 minutes and then washing twice in 0.1xSSC, 0.1% SDS at 50° C to 68° C for 15 minutes."

In view of these amendments, it is respectfully submitted that one skilled in this art would readily understand the scope of the claims.

For the reasons set forth above, it is believed that the rejection of claims 1, 4-7, and 9-11 is rendered moot. Accordingly, withdrawal of the rejection is respectfully requested.

**§112, First Paragraph Rejection:**

**Enablement**

Claims 1, 4, 7, and 11 have been rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. (Paper No. 20070822 at 3). In making the rejection, the Examiner acknowledged that the specification "[is] enabling for an isolated DNA

with SEQ ID NO: 9, which encodes a polypeptide vitamin B6 phosphate phosphatase enzyme of SEQ ID NO: 10 isolated from S. meliloti." (*Id.*).

The Examiner, however, asserted that "the specification ... does not reasonably provide enablement for any DNA that is 70% identical to SEQ ID NO: 9 or any DNA encoding a protein having phosphatase activity and having at least 70% identity to SEQ ID NO: 10 or a fragment thereof ...." (*Id.*).

Initially, we note it is the Examiner's burden to demonstrate that a specification is not sufficiently enabling. *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971). To carry his/her burden, the Examiner must identify and clearly articulate the factual bases and supporting evidence that allegedly establish that undue experimentation would be required to carry out the claimed invention. *Id.* at 370. It is also well established that claims must be separately analyzed. *Ex parte Jochim*, 11 USPQ2d 561 (BPAI 1988).

With a view towards furthering prosecution, claims 1 and 4 (from which claims 7 and 11 depend) have been amended to recite "(c) a DNA sequence encoding a polypeptide having vitamin $B_6$ phosphate phosphatase activity, wherein said polypeptide is at least 95% identical to the amino acid sequence of SEQ ID NO:10" and "(d) a DNA sequence encoding a polypeptide having vitamin $B_6$ phosphate phosphatase activity and is at least 95% identical to the DNA sequence of SEQ ID NO:9."

Moreover, as is well accepted, even a "considerable amount" of experimentation is permissible if it is merely routine or if the specification provides a reasonable amount of guidance. MPEP § 2164.05 and *In re Wands*, 8 USPQ2d 1400,

1404 (Fed. Cir. 1988). In addition, "a patent need not teach, and preferably omits, what is well known in the art." MPEP § 2164.01 (8th ed. Rev. 5, August 2006, p. 2100-187) *citing In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

In view of the foregoing amendments, we note that the specification provides ample disclosure sufficient to inform a skilled artisan that the Applicants enabled the currently claimed vectors, plasmids, and recombinant microorganisms. For example, the specification discloses two examples and four detailed Figures that provide sufficient instruction to one skilled in the art on how to make and use the currently claimed recombinant microorganism, vector, or plasmid encoding vitamin $B_6$ phosphate phosphatase.

Thus, identifying a recombinant microorganism capable of encoding vitamin $B_6$ phosphate phosphatase according to the amended claims is a matter of applying the disclosure in the specification of how to make such microorganisms and testing the vitamin $B_6$ production of the microorganisms compared to *Sinorhizobium meliloti* IFO 14782. (*See* Table 6 of the Specification). It is respectfully submitted that such activity is not undue experimentation.

In view of the foregoing amendments, it is believed that the rejection of claims 1, 4, 7, and 11 is rendered moot. Accordingly, withdrawal of the rejection is respectfully requested.

**Rejection Under 35 USC § 103:**

Claims 1, 4, 7, and 11 have been rejected under 35 USC § 103 as being unpatentable over Capela *et al.*, GenBank Accession No. AL591783 (nucleic acid), August 2001, and GenBank Accession No. Q92SG4 (protein), December 2001) ("Capela") in view of Jang *et al.*, "*Human pyridoxal phosphatase. Molecular cloning, functional expression, and tissue distribution*," J. Biol. Chem., 2003 December 12, 2003; 278(50): 50040-46) ("Jang"). (Paper No. 20070822 at 7).

Capela discloses the isolation of a nucleic acid (GenBank Accession No. AL591783) and a protein (GenBank Accession No. Q92SG4).

Jang discloses that "Pyridoxal 5' -phosphate (PLP) is the coenzymatically active form of vitamin $B_6$ and plays an important role in maintaining the biochemical homeostasis of the body (1,2)." (Page 50040, Col. 1). Jang further discloses that "[t]he PLP phosphatase cDNA was cloned between the BamHI of the bacterial expression vector pQE30 (Qiagen) after PCR amplification. Transformants of *E. coli* M15/pRER4 with the resulting pQE30-hPLPP construct were grown at 37°C in 200 ml of LB medium with 100 *μg*/ml ampicillin and 25 *μg*/ml kanamycin. The plasmid pREP4 constitutively expresses the Lac repressor protein encoded by the *lac*I gene to reduce the basal level of expression (Quiagen). When that culture had grown to an $A_{600}$ of 0.6, isopropyl β-D-thiogalactopyranoside was added to a final concentration of 1mM. After inducing the expression of the PLP phosphatase protein for 16 h at 25°C cells were harvested, washed, and resuspended in 20 ml of 20 mM Tris-HCl buffer, pH 7.4, containing 200 mM NaCl and 20 mM imidazole." (Page 50041, Col. 1).

In making the rejection, the Examiner asserted that Capela discloses that "the protein encoded by the nucleic acid sequence of AL591783 is 99.2% identical to SEQ ID NO: 10 of the instant application, which is **inherently a vitamin B6 phosphate phosphatase protein**." (Paper No. 20070822 at 8) (emphasis original). The Examiner further asserted that "knowledge of the function [of the polypeptide sequence] is not necessary for motivation and the protein of Capela et al., which is 99.2 identical to SEQ ID NO: 10 of the instant application, inherently has said **vitamin B6 phosphate phosphatase function**." (*Id.*) (emphasis original).

The Examiner acknowledged, however, that Capela "do[es] not teach a vector comprising said sequence, [a] transformed host cell and a method of producing said protein in [a] transformed host cell and extraction of cell lysate." (*Id.* at 8-9).

To fill the acknowledged gap in Capela, the Examiner relied on Jang for "teach[ing] human pyridoxal phosphatase or vitamin B6 phosphate phosphatase, its molecular cloning in a vector, functional expression in [an] *E. coli* host cell, and [a] process for producing said protein followed by extraction and purification (p50041, col. 1)." (*Id.* at 9).

The Examiner then contended that "[i]t would have been obvious to one [of] ordinary skill in the art at the time of the invention ... to combine the teachings of Capela et al. and Jang et al. to clone the DNA of Capela et al. by inserting the DNA in a vector, transform an *E. coli* host cell, a process for producing said protein in *E. coli* cells, extract the cell lysate and purification by using the teaching of Jang et al." (*Id.*).

With a view toward furthering prosecution, we note that independent claim 1 has been amended to recite "[a] vector or plasmid comprising an isolated DNA encoding vitamin $B_6$ phosphate phosphatase selected from the group consisting of:

(a) a DNA sequence of SEQ ID NO:9;

(b) a DNA sequence encoding a polypeptide having vitamin $B_6$ phosphate phosphatase activity, which hybridizes under stringent hybridization and stringent washing conditions to the DNA sequence defined in (a) or a fragment thereof, wherein the stringent hybridization and stringent washing conditions comprise hybridizing in 5xSSC, 0.3% SDS, 2% blocking reagent, 0.1% N-lauroylsarcosine, 50% formamide overnight at 42° C and washing twice in 2xSSC, 0.1% SDS at room temperature for 5 minutes and then washing twice in 0.1xSSC, 0.1% SDS at 50° C to 68° C for 15 minutes;

(c) a DNA sequence encoding a polypeptide having vitamin $B_6$ phosphate phosphatase activity, wherein said polypeptide is at least 95% identical to the amino acid sequence of SEQ ID NO:10;

(d) a DNA sequence encoding a polypeptide having vitamin $B_6$ phosphate phosphatase activity and is at least 95% identical to the DNA sequence of SEQ ID NO:9; and

(e) a degenerate DNA sequence of any one of (a) to (c)." And independent claim 4 has been amended to recite "[a] recombinant microorganism of the genus *Sinorhizobium* or *Escherichia*, capable of producing vitamin $B_6$ from vitamin $B_6$ phosphate, wherein said microorganism is transformed with a DNA encoding vitamin $B_6$ phosphate phosphatase selected from the group consisting of:

(a) a DNA sequence of SEQ ID NO:9;

(b) a DNA sequence encoding a polypeptide having vitamin $B_6$ phosphate phosphatase activity, which hybridizes under stringent hybridization and stringent washing conditions to the DNA sequence defined in (a) or a fragment thereof, wherein the stringent hybridization and stringent washing conditions comprise hybridizing in 5xSSC, 0.3% SDS, 2% blocking reagent, 0.1% N-lauroylsarcosine, 50% formamide overnight at 42° C and washing twice in 2xSSC, 0.1% SDS at room temperature for 5 minutes and then washing twice in 0.1xSSC, 0.1% SDS at 50° C to 68° C for 15 minutes;

(c) a DNA sequence encoding a polypeptide having vitamin $B_6$ phosphate phosphatase activity, wherein said polypeptide is at least 95% identical to the amino acid sequence of SEQ ID NO:10;

(d) a DNA sequence encoding a polypeptide having vitamin $B_6$ phosphate phosphatase activity and is at least 95% identical to the DNA sequence of SEQ ID NO:9; and

(e) a degenerate DNA sequence of any one of (a) to (c)."

It is well settled that the Examiner bears the burden to set forth a *prima facie* case of unpatentability. *In re Glaug*, 62 USPQ2d 1151, 1152 (Fed. Cir. 2002); *In re Oetiker*, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992); and *In re Piasecki*, 223 USPQ 785, 788 (Fed. Cir. 1984). If the PTO fails to meet its burden, then the applicant is entitled to a patent. *In re Glaug*, 62 USPQ2d at 1152.

When patentability turns on the question of obviousness, as here, the search for and analysis of the prior art by the PTO should include evidence relevant to

the finding of whether there is a teaching, motivation, or suggestion to select and combine the documents relied on by the Examiner as evidence of obviousness. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1731-32 (2007) (the obviousness "***analysis should be made explicit***" and the teaching-suggestion-motivation test is "***a helpful insight***" for determining obviousness) (emphasis added); *McGinley v. Franklin Sports*, 60 USPQ2d 1001, 1008 (Fed. Cir. 2001). Moreover, the factual inquiry whether to combine documents must be thorough and searching. And, as is well settled, the teaching, motivation, or suggestion to combine should "***be based on objective evidence of record***." *In re Lee*, 61 USPQ2d 1430, 1433 (Fed. Cir. 2002) (emphasis added).

Initially, we note that Jang is ***not*** properly cited as prior art against the present claims. The Examiner acknowledged the present application's claim to benefit to International application no. PCT/EP2003/010575, which claims benefit to EP application no. 02021622.2 filed on **September 27, 2002**. (Paper No. 20070206 at 4). Here, the Jang reference was published in the ***December 12, 2003*** issue of the J. Biol. Chem. - ***over one year after the priority EP application was filed***. In view of the foregoing, the Jang reference cited by the Examiner **is not prior art** to the present application. Because the rejection has failed to fill the acknowledged gaps in Capela, it is insufficient as a matter of law and ***must be*** withdrawn. *See Ex parte Jarvest*, 2001 WL 35811155, *5 (BPAI 2001) (unpublished) ("Hannah is not prior art to the present application. Accordingly, the rejection of the claims as unpatentable over Hannah is reversed."); *Ex parte Brettschneider*, 2007 WL 1537610, *2 (BPAI 2007) (unpublished) ("Brettschneider '930 was published July 4, 2002, ... and is therefore not available as

prior art against the instant invention. Appellant is thus correct that Brettschneider '930 cannot be relied upon in rejecting Appellant's claims ....").

Furthermore, the Examiner again fails to identify where in AL591783 it is disclosed that the translation product defined by the polynucleotide sequence encodes "a vitamin $B_6$ phosphate phosphatase." The Examiner merely asserted that Capela discloses that "the protein encoded by the nucleic acid sequence of AL591783 is 99.2% identical to SEQ ID NO: 10 of the instant application, which is **inherently a vitamin B6 phosphate phosphatase protein**." (Paper No. 20070822 at 8) (emphasis original). The Examiner does not - and cannot - identify where in Capela it is stated, or even suggested, that "a DNA encoding a vitamin $B_6$ phosphate phosphatase is known in the art." As is shown from GenBank Accession No. AL591783 and GenBank Accession No. Q92SG4 (Uniprot), Capela does not indicate any function of the polypeptide sequence, and it is simply characterized as a "hypothetical protein." *See* GenBank Accession No. Q92SG4.

Recognizing these factual gaps, the Examiner seeks refuge in the doctrine of inherency. Although it is well settled that, that which may be inherent is not necessarily known. Obviousness ***cannot*** be predicated on what is unknown. *In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993) ("***That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown.' Such a retrospective view of inherency is not a substitute for some teaching or suggestion supporting an obviousness rejection***.") (citations omitted) (emphasis added).

Indeed, the Examiner's conclusion remains in direct conflict with the IPER, which had AL591783 before it: "The present application relates to a vitamin B6 phosphate phosphatase ... ***which has not been disclosed before in the prior art***." (emphasis added) (Form PCT/Separate Sheet/409 (Sheet 1)); *see also* Form PCT/PEA/409 (concluding that all claims have novelty, inventive step, and industrial applicability). Here, the overwhelming evidence is that Capela does not disclose what is claimed.

For this further reason, the rejection has been rendered moot and must be withdrawn.

Accordingly, for the reasons set forth above, entry of the amendments, withdrawal of the objections and rejections, and allowance of the claims are respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on March 5, 2008.

Charles M. Avigliano, Reg. No. 52,578

Respectfully submitted,

By: Charles M. Avigliano

Charles M. Avigliano
Registration No. 52,578
BRYAN CAVE LLP
1290 Avenue of the Americas
33rd Floor
New York, NY 10104-3300
Phone: (212) 541-2000
Fax: (212) 541-4630